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A MATHEMATICAL MODEL FOR THE STUDY OF HEMORRHAGIC SHOCK AND FLUID RESUSCITATION: THE SYSTEMIC AND PULMONARY VASCULATURE

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Division of Military Trauma Research

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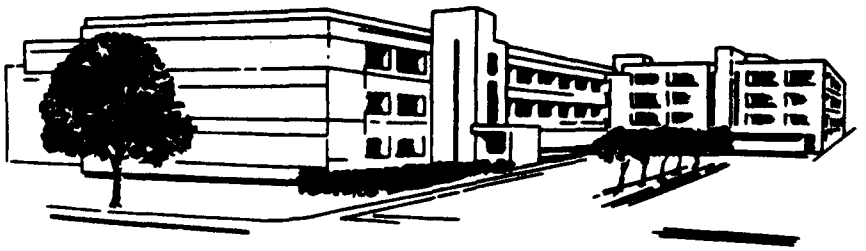

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A MATHEMATICAL MODEL FOR THE STUDY OF HEMORRHAGIC SHOCK AND FLUID RESUSCITATION: THE SYSTEMIC AND PULMONARY VASCULATURE – TAMMY J. DOHERTY

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for Barbara A. Wilson, MAJ, MS, DCA
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In systemic and pulmonary circuit models, the number and configuration of vascular compartments may affect predictions of vascular volume and blood flow. In this paper, we consider various models of the pulmonary and systemic vascular circuits to identify models appropriate for studies of hemorrhage and fluid resuscitation. We found that at least one pulmonary vascular compartment, made up of one resistance and one capacitance element, was required to describe the response of pulmonary blood volume to changes in pulmonary inflow rate (i.e., right heart output). Incorporation of additional pulmonary vascular segments did not alter predictions of pulmonary volume or flow rate. Therefore, one lumped pulmonary vascular compartment appears to be sufficient. It may be necessary to incorporate multiple pulmonary vascular segments, however, for studies of pulmonary transcapillary exchange or cardiovascular control. The initial model for the systemic circuit included a separate capillary compartment for studies of transcapillary exchange as well as variable resistance and compliance elements for studies of cardiovascular control. Model identification for the systemic circulation focused on the most appropriate number of parallel vascular pathways for predicting the response of systemic outflow (i.e., venous return) to changes in systemic inflow (i.e., left heart output). At least two separate parallel pathways were required to predict systemic outflow rate because of differences in the distribution time constant between skeletal muscle and other vascular beds. Based on vascular responses to epinephrine and norepinephrine, the systemic circulation was divided into three lumped vascular pathways: 1) skeletal muscle, 2) vital organs (heart, brain, and diaphragm), and 3) other nonmuscle, nonvital organs (spleen, liver, pancreas, small intestine, fat, skin, and kidney). Results presented in this paper suggest that the one-segment pulmonary model and the three-pathway systemic model are the simplest possible models for the study of cardiovascular responses to hemorrhage and fluid resuscitation.

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ABSTRACT

In systemic and pulmonary circuit models, the number and configuration of vascular compartments may affect predictions of vascular volume and blood flow. In this paper, we consider various models of the pulmonary and systemic vascular circuits to identify models appropriate for studies of hemorrhage and fluid resuscitation. We found that at least one pulmonary vascular compartment, made up of one resistance and one capacitance element, was required to describe the response of pulmonary blood volume to changes in pulmonary inflow rate (i.e., right heart output). Incorporation of additional pulmonary vascular segments did not alter predictions of pulmonary volume or flow rate. Therefore, one lumped pulmonary vascular compartment appears to be sufficient. It may be necessary to incorporate multiple pulmonary vascular segments, however, for studies of pulmonary transcapillary exchange or cardiovascular control. The initial model for the systemic circuit included a separate capillary compartment for studies of transcapillary exchange, as well as variable resistance and compliance elements for studies of cardiovascular control. Model identification for the systemic circulation focused on the most appropriate number of parallel vascular pathways for predicting the response of systemic outflow (i.e., venous return) to changes in systemic inflow (i.e., left heart output). At least two separate parallel pathways were required to predict systemic outflow rate because of differences in the distribution time constant between skeletal muscle and other vascular beds. Based on vascular responses to epinephrine and norepinephrine, the systemic circulation was divided into three lumped vascular pathways: 1) skeletal muscle, 2) vital organs (heart, brain, and diaphragm), and 3) other nonmuscle, nonvital organs (spleen, liver, pancreas, small intestine, fat, skin, and kidney). Results presented in this paper suggest that the one-segment pulmonary model and the three-pathway systemic model are the simplest possible models for the study of cardiovascular responses to hemorrhage and fluid resuscitation.

key words: model, systemic circulation, pulmonary circulation.

A Mathematical Model for the Study of Hemorrhagic Shock and Fluid Resuscitation: The Systemic and Pulmonary Vasculature

-- Tammy J. Doherty

INTRODUCTION

In a previous paper[1], we identified a model of the left ventricle for studies of hemorrhage and fluid resuscitation. In this paper, we attempt to identify models of the pulmonary and systemic vasculature for the same purpose. Previous mathematical models of the circulation, that might be used to study hemorrhage and resuscitation, range from simple lumped-parameter models containing only a few compartments[2-3], to complex models involving multiple parallel circuits made up of multiple vascular segments in each circuit[4-8]. To determine which model or level of model complexity is most appropriate for studies of hemorrhage and fluid resuscitation, predictions of blood volume and blood flow, generated by models of various complexity are compared.

INITIAL ASSUMPTIONS

Certain initial assumptions must be made to facilitate the formulation of model equations. The model assumptions selected for this purpose have been used in previous cardiovascular system models[1-7], and are listed below:

1. blood is an incompressible fluid.
2. blood flow around the circulation is non-pulsatile.
3. compartments mix instantaneously
4. mass and volume are conserved within each compartment

We also assume that the pulmonary and systemic circuits may be represented by vascular segments connected in serial and/or parallel, and that each vascular segment is made up of simple resistance and capacitance elements.

Resistance Elements

The movement of fluid from one point to another is driven by hydrostatic pressure gradients. These gradients are required because fluid moving through the vasculature loses energy due to viscous and nonconservative inertial forces. These energy losses are described by a flow resistance term (R_{ab}) which is defined as the ratio of the total hydrostatic pressure gradient (P_a-P_b) to the average volumetric blood flow rate ($Q_{v,ab}$) between two points (a and b):

$$R_{ab} = \frac{(P_a - P_b)}{Q_{v,ab}} \quad (1)$$

Resistance to blood flow depends on many factors including vessel tone, diameter, taper, curvature, and branching, as well as fluid viscosity and inertiance. In the models described here, resistance may be altered to reflect changes in fluid and vessel wall properties.

Because vessel walls are elastic, external hydrostatic pressures may affect blood flow. For this reason, transmural rather than absolute hydrostatic pressures are inserted into the resistance-pressure-flow equation. In collapsible vessels (e.g., in pulmonary vessels and systemic veins), transmural pressures must be greater than or equal to zero. This condition eliminates the need to use a 3-pressure model[9] to describe flow in collapsible vessels.

Capacitance Elements

Vascular capacitance describes the ability of the vascular segment to store blood. Capacitance is most often described by the relationship between vascular pressure and volume. Vascular compliance for compartment i (C_i) is defined as the rate of change in vascular volume with respect to pressure:

$$C_i = \frac{dV_i}{dP_i} \quad (2)$$

Pressure-volume relationships for vascular specimens are characteristically nonlinear[10]. Compliance is generally high at low volumes, decreasing as volume increases. Particularly in the veins, compliance depends not only on compartment volume, but on rates of volume change as well. It is reasonable to assume that lumped vascular compartment pressure-volume relationships behave in similar fashion. In practice, measuring lumped compartment pressure-volume relationships is difficult because controlling compartment volume and seepage, measuring a "representative" compartment pressure, and accessing certain structures without altering the state of the system are also difficult. In this study, empirically-determined single-valued compliance estimates will be used as initial values. However, it is assumed that compliance may be altered to reflect changes in vessel tone, vascular pressure and volume, and rates of vascular pressure and volume change.

THE PULMONARY VASCULATURE

Simple models of the overall circulation sometimes neglect the pulmonary pathway by lumping the left and right hearts together with the pulmonary circuit as a single compartment[1,2,11]. Most models, however, consider separate heart compartments, and one or more pulmonary vascular segments[4,6,12,13]. Multiple vascular segments may be required, depending on the purpose or the model[9,14-16]. In this section, simple models of the pulmonary circulation are examined to determine whether a discrete pulmonary pathway is necessary for macroscopic hemodynamic studies and, if so, the smallest number of vessel segments that can be used to represent it. The effects of gravity on pulmonary pressure are neglected by assuming that simulated subjects are resting in a horizontal position. The effects of respiration on pulmonary blood flow are neglected except for considerations of transmural hydrostatic pressures.

The distribution time constant (i.e., resistance multiplied by compliance) for the pulmonary circulation is small. Defares[13] estimates pulmonary compliance to be 0.57 $ml \cdot kg^{-1} \cdot mm\ Hg^{-1}$ and total pulmonary resistance to be 0.093 $mm\ Hg \cdot kg \cdot min \cdot ml^{-1}$, which yields a distribution time constant of 0.053 minutes or 3.2 seconds. Thus, pulmonary outflow rates are expected to equilibrate to new pulmonary inflow rates in approximately 12-15 seconds. If the temporal response time of the model is longer than 15 seconds, and blood flow is the only variable of interest, then the pulmonary circuit could be modelled as a lumped flow path in which outflow rates are assumed to equal inflow rates instantaneously. However, if estimates of blood volume are also of interest, then the capacitance of the pulmonary circulation cannot be neglected. Although flow equilibration occurs rapidly (i.e., approximately 15 seconds), the change in volume resulting from temporarily mismatched inflow and outflow rates may be significant, as shown below.

The relationship between inflow and outflow rates, for a single-segment model of the pulmonary vasculature (Figure 1), is given by:

$$C_P R_P \frac{dQ_{out}}{dt} + \Delta Q_{out} = \Delta Q_{in} \qquad (3)$$

where Δ indicates a change from the control level. Changes in pulmonary outflow rate may be obtained by solving Equation 3 for ΔQ_{out}:

$$\Delta Q_{out} = \Delta Q_{in}(1 - e^{-\frac{t}{C_P R_P}}) \quad (4)$$

Changes in pulmonary volume may be obtained by integrating (ΔQ_{in}-ΔQ_{out}) over time:

$$\Delta V_P = \Delta Q_{in} C_P R_P (1 - e^{-\frac{t}{C_P R_P}}) \quad (5)$$

According to this equation (using C_P=0.57ml·kg^{-1}·mm Hg^{-1} and R_P=0.093 mm Hg·kg·min·ml^{-1}), at steady state (i.e., t=∞), the decrease in pulmonary volume corresponding to a 35 ml/kg·min (50%) decrease in inflow rate is approximately 2.2 ml/kg (14%). Depending on the application of the model, this change in pulmonary volume could be significant. Thus, it appears that at least one capacitance element is required.

Next, predictions of pulmonary volume and outflow rate generated by the one-vessel model (Figure 1) were compared to predictions generated by a two-vessel model (Figure 2). Expressions for ΔQ_{out} and ΔV_P for the one-segment model are provided in Equations 4 and 5. The expression relating Q_{out} and Q_{in} for the two-segment model is given by:

$$\frac{d^2 Q_{out}}{dt^2} + (\alpha_{AP} + \alpha_{VP} + \alpha_X)\frac{dQ_{out}}{dt} + \alpha_{AP}\alpha_{VP}\Delta Q_{out} = \alpha_{AP}\alpha_{VP}\Delta Q_{in} \quad (6)$$

where:

$$\alpha_{AP} = \frac{1}{R_{AP} C_{AP}}, \qquad \alpha_{VP} = \frac{1}{R_{VP} C_{VP}}, \qquad \alpha_X = \frac{1}{R_{AP} C_{VP}} \quad (7)$$

The change in pulmonary outflow rate for this model is obtained by solving Equation 6 for ΔQ_{out}:

$$\Delta Q_{out} = \Delta Q_{in}\left(1 + \frac{\lambda_1 e^{\lambda_1 t}}{(\lambda_2 - \lambda_1)} + \frac{\lambda_2 e^{\lambda_2 t}}{(\lambda_1 - \lambda_2)}\right) \quad (8)$$

where:

$$\lambda_{1,2} = \frac{-(\alpha_{AP} + \alpha_{VP} + \alpha_X) \pm \sqrt{(\alpha_{AP} + \alpha_{VP} + \alpha_X)^2 - 4\alpha_{AP}\alpha_{VP}}}{2} \qquad (9)$$

Changes in V_P, for the two-vessel model, are computed by taking the integral of the difference (ΔQ_{in} - ΔQ_{out}) over time:

$$\Delta V_P = \Delta Q_{in}\left(- \frac{\alpha_{AP}\alpha_{VP}e^{\lambda_1 t}}{\lambda_1^2(\lambda_1 - \lambda_2)} - \frac{\alpha_{AP}\alpha_{VP}e^{\lambda_2 t}}{\lambda_2^2(\lambda_2 - \lambda_1)} \right) \qquad (10)$$

Changes in pulmonary volume and outflow rates were computed from Equations 4, 5, 8, and 10, for a 35 ml/kg·min (50%) increase in inflow rate, using resistance and capacitance from Defares[13] (Tables 1 and 2). There were small, transient differences in both volume and outflow rates predicted by the two models (Figure 3) which can probably be neglected. Alterations in parameter values of ±50% did not change these results. Based on these analyses, a one-vessel model of the pulmonary circuit appears sufficient to describe changes in volume and flow rate resulting from changes in inflow rate. Extending the model to two or more vascular segments may be required, however, for considerations of pulmonary transcapillary flux or cardiovascular control.

THE SYSTEMIC VASCULATURE

There have been many different representations of the systemic circulation presented over the years. These vary from a simple, three-element network model consisting of arterial compliance, venous compliance, and the resistance between them[1,2,7,11-13,17-21], to elaborate representations that divide the systemic vasculature into two or more parallel circuits, with one or more vascular segments in each circuit[3-7,22-24]. Eventually, any realistic model of the systemic vasculature used to predict responses to hemorrhage and fluid administration must consider vascular control mechanisms as well as transcapillary fluid exchange. Such a model must include pre- and post-capillary resistances, venous compliance, estimates for capillary hydrostatic pressure (for transcapillary exchange), and estimates for volume and pressure in the large arteries (for baroreceptor input). One arrangement of model components that would fit these requirements is shown in Figure 4.

A strong motivation for expanding the model in Figure 4 to include two or more parallel flow paths (Figure 5) is the difference in compliance between parallel vascular beds, and the effect of this compliance difference on venous return[25-26]. Permutt and Wise[27] examine the effects of shifting a small amount of blood from a pathway with a large time constant for drainage (τ=CR, where C is compliance and R is resistance of the pathway), such as non-muscle circulations (subscript n), to a pathway with a smaller time constant, such as skeletal muscle (subscript m). From Equations 1 and 2, flow rates through the paths are:

$$Q_m = \frac{V_m - V_{m_o} - P_{RA}C_m}{C_m R_m} \quad and \quad Q_n = \frac{V_n - V_{n_o} - P_{RA}C_n}{C_n R_n} \qquad (11)$$

where P_{RA} is right atrial pressure. Assuming that P_{RA} is constant, differentiation yields:

$$dQ_m = \frac{dV_m}{\tau_m} \quad and \quad dQ_n = \frac{dV_n}{\tau_n} \qquad (12)$$

The total outflow rate from the systemic circulation (Q_{out}) is the sum of Q_m and Q_n. Thus:

$$dQ_{out} = \frac{dV_m}{\tau_m} + \frac{dV_n}{\tau_n} \qquad (13)$$

There is evidence that τ_n is significantly larger than τ_m[25]. Thus, a small shift of blood flow from nonmuscle to muscle beds ($dV_m = -dV_n$), results in a net increase in total blood flow out of the network (venous return).

The most obvious means for obtaining the shift in blood flow from nonmuscle to muscle beds is to increase the arteriovenous resistance of the nonmuscle bed while decreasing resistance in the muscle bed. In both open and closed-circuit models of the systemic vasculature (Figures 4 and 5, Table 3), altering arteriovenous resistances in this manner results in an increase in total systemic outflow (Figure 6). In the open circuit model, however, this increase is short-lived; for the simulated 25% change in muscle and nonmuscle vascular bed resistances, systemic outflow returned to normal values within 20 seconds. The sustained increase in systemic outflow obtained with the closed-circuit model was possible only by assuming that systemic inflow (i.e., cardiac output) was equivalent to systemic outflow (i.e., venous return). In general,

Starling's Law of the heart guarantees that this condition is met for normal physiologic loads.

In our model, an increase in nonmuscle resistance, without a simultaneous decrease in muscle bed resistance, did not result in increased systemic outflow. Flow diverted from the nonmuscle bed does not necessarily pass through the muscle bed. Instead, because the arterial compartment is compliant, some of the flow diverted from the nonmuscle bed is stored in the large arteries, and total systemic outflow actually decreases. This result is inconsistent with predictions generated by Coleman's[26] two-pathway model. In the Coleman model[26], an increase in systemic outflow occurs without a change in muscle bed resistance. The reason for this increase in systemic outflow is that the model does not include a compliant arterial compartment, and all of the flow diverted from the visceral bed is assumed to flow through the less compliant peripheral bed. Even though predictions of the Coleman model agree with data in which the aorta was occluded distal to the subclavian artery in dogs[28], we believe that a compliant arterial compartment is appropriate. The most likely explanation for the increase in venous return during episodes of increased nonmuscle bed resistance (no applied change to muscle bed resistance) is that capillary networks in the muscle bed open to accommodate increased flow. This increased capillary recruitment may be accomplished in the present model by a decrease in muscle bed vascular resistance.

In a system of parallel vascular beds, flow redistribution might affect not only systemic outflow rates, but net intra-to-extravascular fluid and solute exchange as well. Decreasing flow to a vascular bed results in a decline in capillary hydrostatic pressure. According to the Landis-Starling Equation[29-30]:

$$J = k\left[(P_C - P_I) - (\Pi_C - \Pi_I)\right] \qquad (14)$$

transcapillary fluid movement from the capillary (subscript C) to the interstitial (subscript I) compartment is approximately proportional to hydrostatic (P) and osmotic (Π) pressure differences across the capillary wall. From this equation, it follows that a decrease in capillary pressure would result in an increase in extravascular-to-intravascular fluid movement. If capillary hydraulic conductivity (proportionality coefficient k in Equation 14) is higher in one bed than another, then diverting flow from the high permeability bed to the low permeability bed should favorably affect transcapillary fluid exchange. Because capillary hydrostatic pressures are affected by compliances in the systemic circuit, any compliance difference between the two beds will augment or attenuate the response.

From the preceding discussion, it is evident that blood flow amplification and enhancement of transcapillary exchange, by diversion of flow from compliant to less compliant beds, is possible in theory. In addition, there is direct evidence that blood flow redistribution from visceral to peripheral beds occurs after epinephrine infusion[25]. Unfortunately, there is no direct evidence for this type of flow redistribution after hemorrhage. Table 4 shows measured values of organ blood flow after hemorrhage (from Bellamy et al. 1984[31]). As expected, cardiac and cerebral blood flows are well protected while flow in peripheral beds declines. Due to the high variability in measured values, however, it is uncertain whether blood is preferentially distributed to one peripheral vascular bed over another.

If diversion of flow from one vascular bed to another, or preferential changes in compliance do occur in the response to hemorrhage or fluid resuscitation, it is probably achieved by selective sympathetic or hormonal control. Based on this assumption, the most appropriate model for the systemic circulation may incorporate parallel flow pathways lumped on the basis of receptor sites for vasoactive substances. Alpha receptors, stimulated by norepinephrine and epinephrine are present in the smooth muscle of arterioles throughout the vasculature, as well as in veins of the splanchnic and skin circulations. Stimulation of these receptors causes vascular constriction. $Beta_2$ receptors, stimulated by circulating epinephrine, are located in the arterioles of skeletal muscle. These receptors are noticeably absent in skin, splanchnic and kidney circulations. Stimulation of these receptors causes vascular relaxation. Coronary and cerebral circulations are relatively insensitive to sympathetic stimulation. Thus, the systemic circulation may be separated into three pathways based on response to sympathetic factors:

1) Vital Organs: heart, brain, diaphragm.
2) Skeletal Muscle
3) Non-Muscle: Spleen, liver, pancreas, small intestine, fat, skin, kidney.

A schematic of the systemic circulation based on these considerations is presented as Figure 7.

SUMMARY AND CONCLUSIONS

The number and arrangement of pulmonary and systemic vascular segments affects predictions of pulmonary and systemic vascular volumes and flow. In the models tested, vascular segments were made up of simple, variable resistance and capacitance elements. One vascular segment consisting of one resistance and one compliance element (Figure 1) was sufficient to describe pulmonary volume and flow. Expansion of the pulmonary model to

include separate pulmonary artery, capillary, and vein segments may be required to estimate pulmonary transcapillary fluid and solute exchange.

To facilitate studies of cardiovascular control and transcapillary exchange mechanisms, the initial one-path model of the systemic vasculature (Figure 4) was designed to include capillary compartments as well as variable resistance and compliance elements. For the systemic circulation, model development focused on the most appropriate number of parallel pathways. At least two separate pathways were required to account for differences in distribution time constants between muscle and nonmuscle beds. When two pathways were considered, diverting blood flow from the high-compliance to the low-compliance pathway enhanced total systemic outflow (i.e., venous return). This increase in systemic outflow rate was transient in nature unless the model included a mechanism so that systemic inflow (i.e., cardiac output) equaled systemic outflow (i.e., venous return). The healthy mammalian heart is capable of assuring that cardiac output equals venous return for normal physiologic loads. Three or more parallel vascular flow pathways were required to account for differences in vascular response to sympathetic agents. In the end, lumping of systemic vascular beds into parallel pathways (vital organs, muscle, and nonmuscle) was based on differences in vascular response to epinephrine and norepinephrine.

In studies of the pulmonary and systemic circuit models, simple variable resistance and capacitance elements were used. Values for resistance and compliance are strongly controlled by neural and humoral factors. Resistance is also affected by vascular geometry, vascular volume, fluid viscosity, and blood flow rate. Compliance depends primarily on vessel tone which may be affected by vascular volume and/or vascular pressure, as well as rates of pressure and/or volume change. Identification of equations describing resistance and compliance changes during changes in blood volume and blood osmolarity is beyond the scope of this paper. However, it is hoped that, in the future, the model developed here will be used for this purpose.

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TABLE 1. Initial conditions and parameter values for the 1-segment pulmonary circuit model (Figure 1).

variable	value
Q_{in}	70 $ml \cdot kg^{-1} \cdot min^{-1}$
Q_{out}	70 $ml \cdot kg^{-1} \cdot min^{-1}$
V_P	9.04 $ml \cdot kg^{-1}$
P_P	9.692 mm Hg
R_P	0.1385 mm $Hg \cdot kg \cdot min \cdot ml^{-1}$
C_P	0.181 $ml \cdot kg^{-1} \cdot mm\ Hg^{-1}$

TABLE 2. Initial conditions and parameter values for the 2-segment pulmonary circuit model (Figure 2).

variable	value
Q_{in}	70 $ml \cdot kg^{-1} \cdot min^{-1}$
Q_{out}	70 $ml \cdot kg^{-1} \cdot min^{-1}$
V_{AP}	1.7 $ml \cdot kg^{-1}$
P_{AP}	16.159 mm Hg
R_{AP}	0.1393 mm $Hg \cdot kg \cdot min \cdot ml^{-1}$
C_{AP}	0.061 $ml \cdot kg^{-1} \cdot mm\ Hg^{-1}$
V_{VP}	7.34 $ml \cdot kg^{-1}$
P_{VP}	6.405 mm Hg
R_{VP}	0.0915 mm $Hg \cdot kg \cdot min \cdot ml^{-1}$
C_{VP}	0.120 $ml \cdot kg^{-1} \cdot mm\ Hg^{-1}$

TABLE 3. Initial conditions and parameter values for the 2-pathway systemic circuit model (Figure 5).

variable	value
Q_{in}	70 $ml \cdot kg^{-1} \cdot min^{-1}$
Q_{out}	70 $ml \cdot kg^{-1} \cdot min^{-1}$
P_A	100 mm Hg
C_A	0.0375 $ml \cdot kg^{-1} \cdot mm\ Hg^{-1}$
$V_{n,V}$	33.6 $ml \cdot kg^{-1}$
$V_{m,V}$	11.2 $ml \cdot kg^{-1}$
$C_{n,V}$	1.056 $ml \cdot kg^{-1} \cdot mm\ Hg^{-1}$
$C_{m,V}$	0.352 $ml \cdot kg^{-1} \cdot mm\ Hg^{-1}$
$P_{i,V}$	6.29 mm Hg
$R_{i,A}$	2.6774 $mm\ Hg \cdot kg \cdot min \cdot ml^{-1}$

TABLE 4. Changes in organ blood flow after hemorrhage (from Bellamy[31]).

Vascular Bed	% of control
Heart	110%
Brain	100%
Muscle	45%
Mesentery	22%
Spleen	40%
Skin	20%
Kidney	10%
Hepatic Artery	55%
Portal Vein	43%

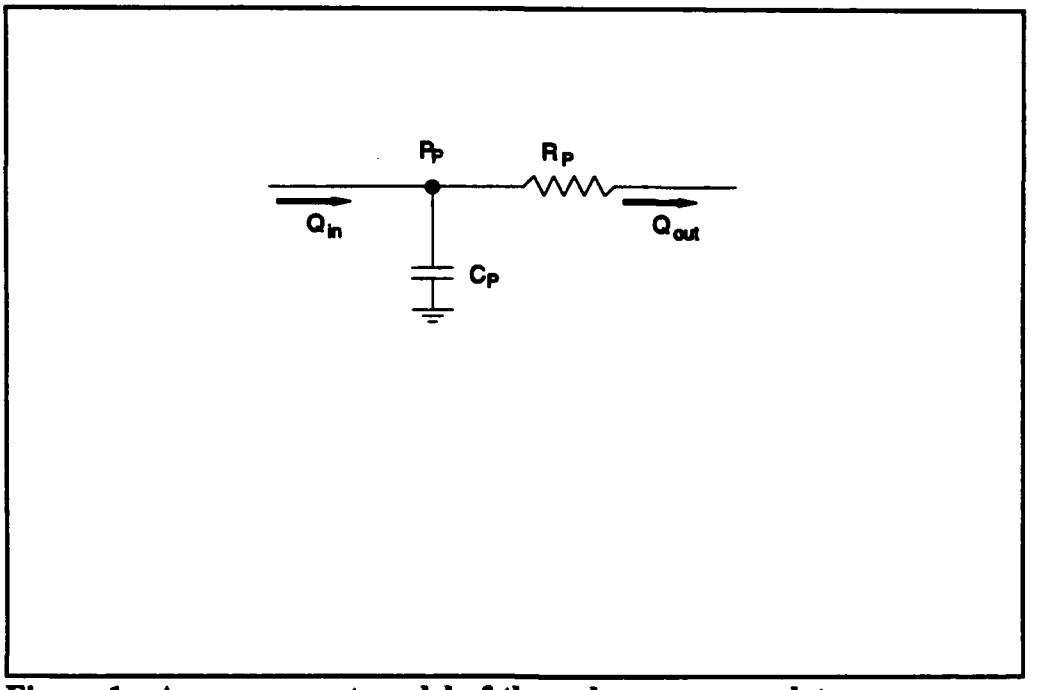

Figure 1. A one-segment model of the pulmonary vasculature.

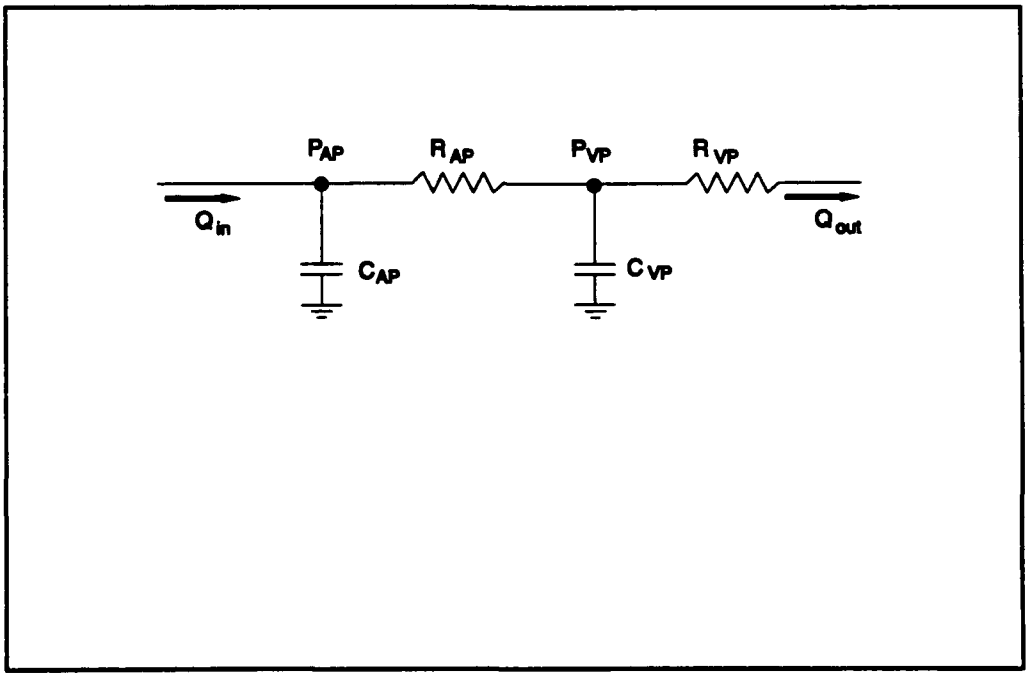

Figure 2. Two-segment model of the pulmonary vasculature.

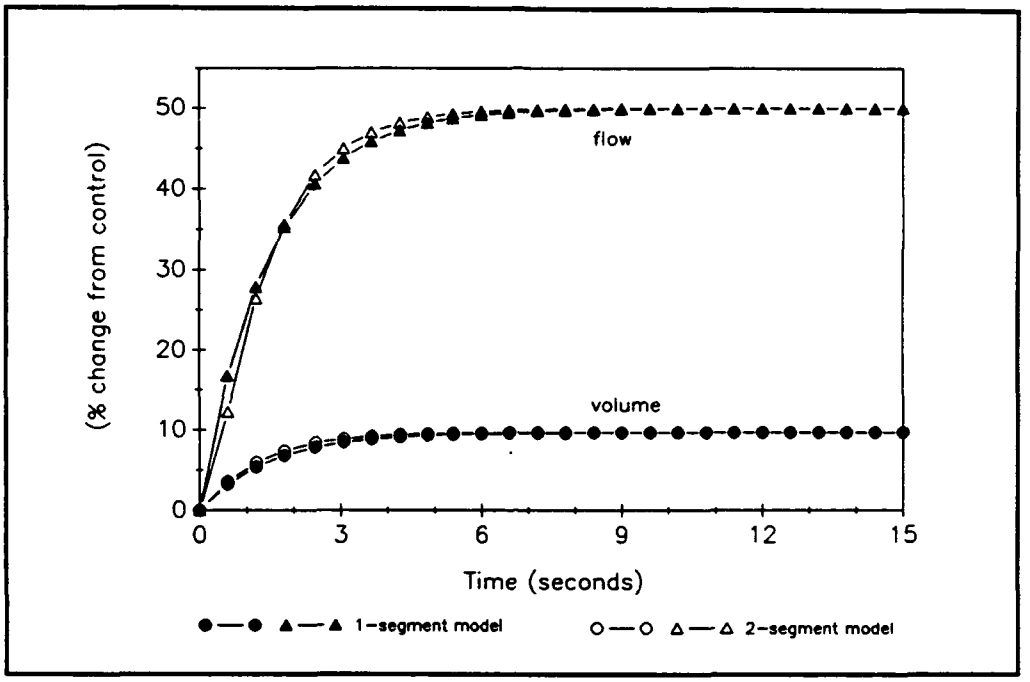

Figure 3. Predicted pulmonary volume and outflow response to a 50% change in pulmonary inflow rate.

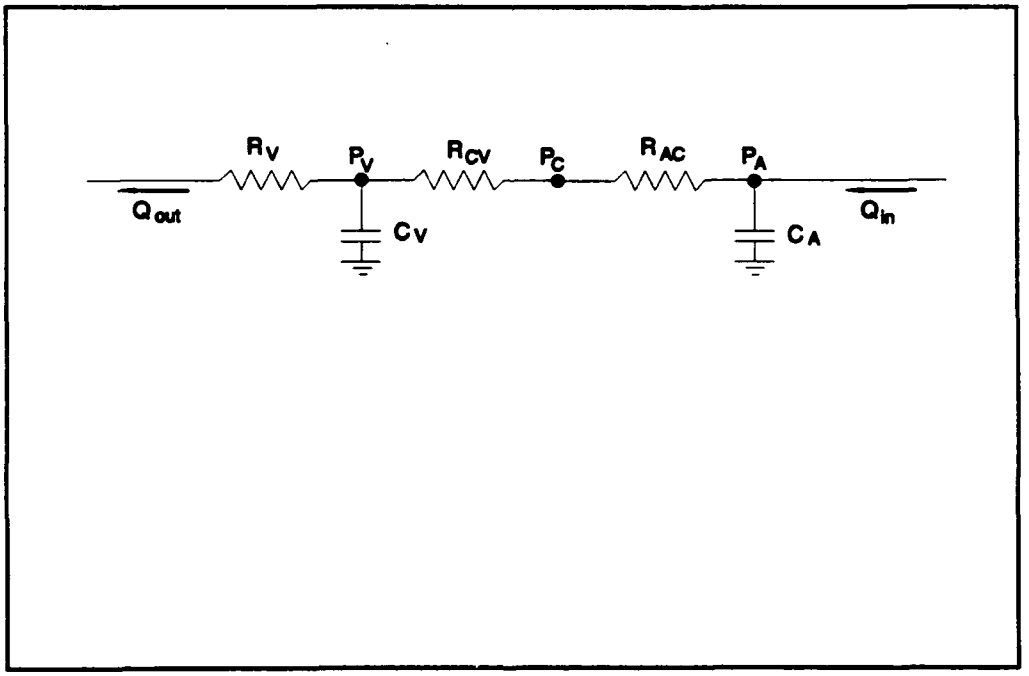

Figure 4. A model of the systemic circulation consisting of one vascular pathway from left ventricle to right atrium.

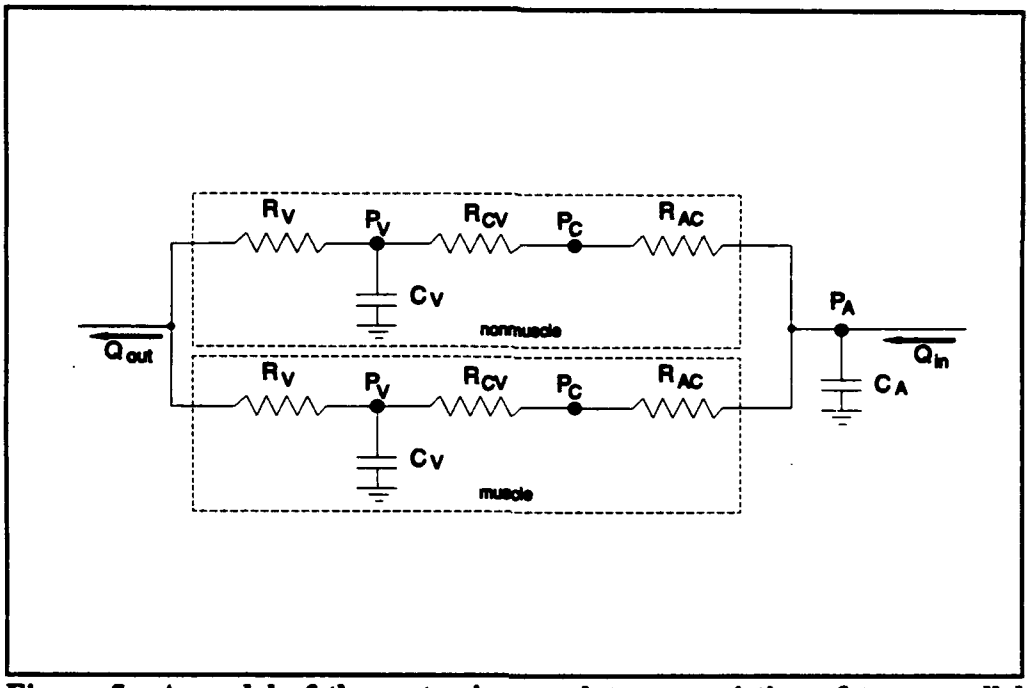

Figure 5. A model of the systemic vasculature consisting of two parallel vascular pathways.

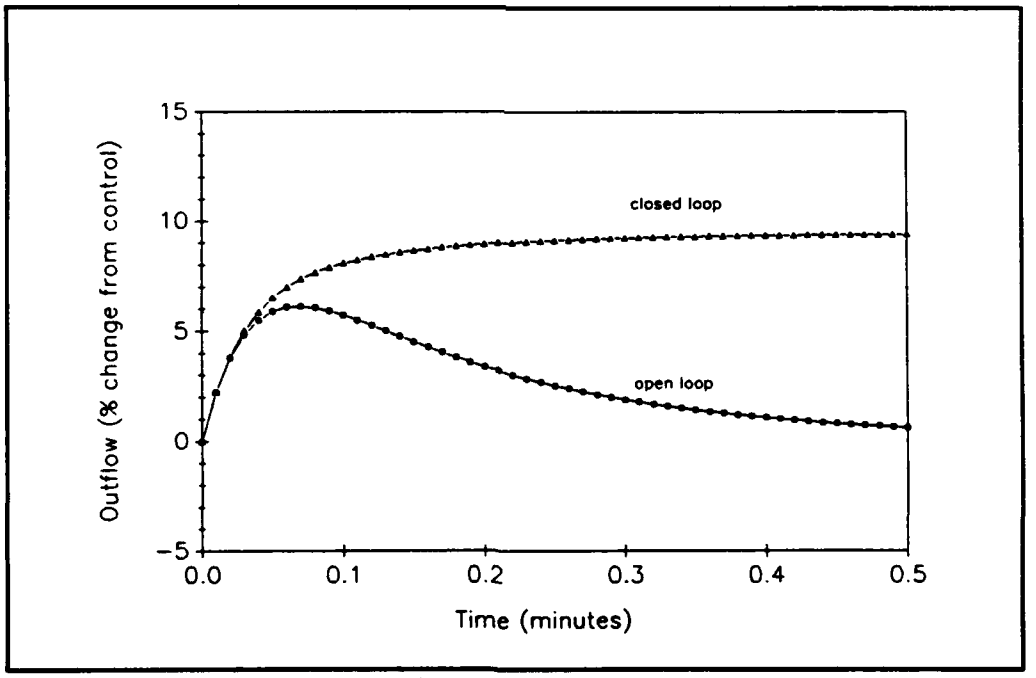

Figure 6. Predicted systemic outflow response to a 25% increase in nonmuscle bed vascular resistance and a 25% decrease in muscle bed vascular resistance.

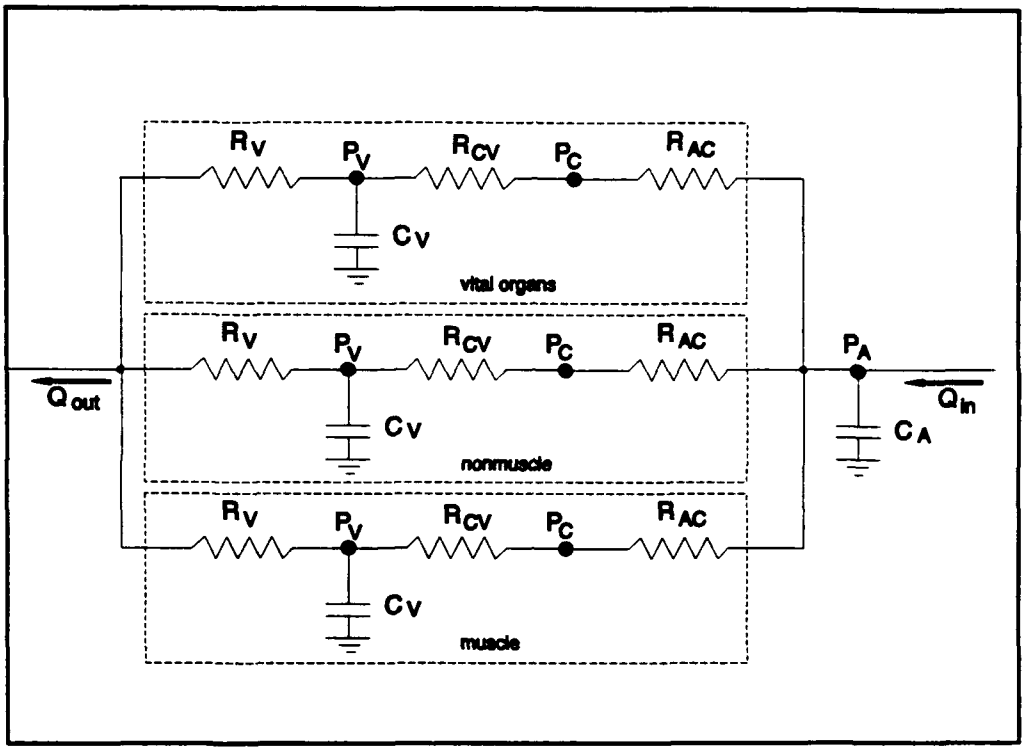

Figure 7. A model of the systemic circulation consisting of three parallel vascular pathways.

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